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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/813,463	01/11/2002	Kenneth G. Warren	098810/0278740	8427

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EXAMINER	
CHERNYSHEV, OLGA N	
ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 05/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/813,463	WARREN ET AL.	
	Examiner	Art Unit	
	Olga N. Chernyshev	1646	

-- The MAILING DATE of this communication app ars on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *16-20* is/are pending in the application.

4a) Of the above claim(s) *16 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 January 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group II in Paper No. 15 is acknowledged.

Claims 16-17 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 15.

Claims 18-20 are under examination in the instant office action.

Priority

2. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 and/or 121 as follows:

This application is claiming the benefit of a prior filed nonprovisional application under 35 U.S.C. 120, 121, or 365(c). Copendency between the current application and the prior application is required.

The instant application claims priority to an earlier US application 09/055,263. However, the instant application was granted filing date of 01/11/2002, which precludes priority to 09/055,263, for which a patent was issued on 06/26/2001. See copies of PALM Application Number Information regarding 09/813,463 and 09/055,263 attached to the instant office action.

35 U.S.C. 120, Benefit of earlier filing date in the United States, states that

> An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or on an

application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

Therefore, for art purposes the filing date of the instant application is considered to be 01/11/2002.

Drawings

3. Figures 11a-11d of the instant application are not in compliance with 37 C.F.R. § 1.84(u) (1), which states that when partial views of a drawing which are intended to form one complete view, whether contained on one or several sheets, must be identified by the same number followed by a capital letter. Applicant is reminded that once the drawings are changed to meet the separate numbering requirement of 37 C.F.R. § 1.84(u) (1), the specification should be amended to change the Brief Description of the Drawings and the rest of the specification to refer to each Figure accordingly. If, for example, Figure 11 is renumbered as Figures 11A-11D, then the Brief Description and all the references to these figures in the specification must refer to these figures in the same manner.

Specification

4. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. § 1.821 through 1.825 for the following reasons. Specifically, the text of pages 5-6, 12-13 and 15-16 of the instant specification contains sequences, which are not properly identified. In case these

sequence are new, Applicant needs to provide a substitute computer readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, a substitute paper copy of that "Sequence Listing", an amendment directing the entry of that paper copy into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d). The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (SEQ ID NO:) be made in the specification wherever a reference is made to that sequence. For rules interpretation Applicant may call (703) 308-1123. See M.P.E.P. 2420-2435.

5. The text on page 13, lines 12 and 17 is not in compliance with the requirements for Sequence Identifiers (see MPEP 2422.03). The appropriate format for sequence identifiers is SEQ ID NO: X, wherein "X" is the sequence number. Appropriate correction is required.

6. The use of the trademark has been noted in this application, see page 20, lines 22 and 29. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

7. Claims 19 and 20 are objected to because of the following informalities: claims 19 and 20 depend from cancelled claims 1 and 3. Appropriate correction is required.

For purpose of examination claims 19 and 20 are treated as being depended from claim 18.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 18-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of predicting therapeutic efficacy of treatment of multiple sclerosis (MS) with a peptide of 8 to 25 amino acids and having a sequence contained within SEQ ID NO: 1, provided that the peptide is capable of neutralizing or modulating the production of anti-myelin basic protein, by screening a multiple sclerosis patient for the presence of an HLA-DR2 haplotype, does not reasonably provide enablement for a method of predicting therapeutic efficacy of treatment of MS with a peptide of 8 to 25 amino acids from a fragment 61-106 of SEQ ID NO: 1, including substitutions, additions or deletions thereof, by screening an MS patient for the presence of an HLA-DR2 haplotype. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Claims 18-20 are directed to a method of predicting therapeutic efficacy of treatment of multiple sclerosis with a peptide of 8 to 25 amino acids from a fragment 61-106 of SEQ ID NO: 1, including substitutions, additions or deletions thereof, provided that the peptide is capable of neutralizing or modulating the production of anti-myelin basic protein, by screening a MS patient

for the presence of an HLA-DR2 haplotype. However, the instant specification fails to provide enough guidance for one skilled in the art on how to practice the instant method, thereby requiring undue experimentation to discover how to use Applicant's invention, as currently claimed.

The factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. In re Wands, 8 USPQ2d, 1400 (CAFC 1988).

The nature of the invention is the demonstration that administration of a peptide disclosed on page 5, line 14 of the instant specification, to MS patients leads to neutralization of anti-myelin basic protein and, consequently, to the treatment of MS. The sequence disclosed on page 5, line 14 appears to correspond to the fragment 27-33 of SEQ ID NO: 1 of the instant specification (see page 15, for example) and also to the fragment 88-94 of the sequence of myelin basic protein (MBP), which is known in the prior art (see US Patent 6,379,670, columns 33 and 35, SEQ ID NO: 2). The state of the art is such that it recognizes presence of HLA-DR2 allele as a risk factor for MS (Hauser et al., 1989, Neurology, 39, pp.275-277, see page 275, abstract and the first paragraph specifically). Salvetti et al. (Eur. J. Immunology, 1993, 23, pp.1232-1239), among others, describe a possible mechanism of pathogenesis of MS, which includes a specific response of T-cells against the middle portion of MBP (88-99) in $DR2^+$ patients (see page 1237, last paragraph and Table 3). Thus, the art recognizes a connection

between MS, HLA-DR2 haplotype and the specific T-cell response to MBP in MS patients carrying the HLA-DR2 allele.

However, the instant invention, as claimed, encompasses a method of predicting efficacy of treatment of MS with a peptide, which is not described in the instant specification, as filed, because SEQ ID NO: 1 consists of 46 amino acids. One skilled in the art would clearly not be able to practice the claimed method because the instant specification fails to teach how to treat MS by administration of a peptide "having a sequence contained within amino acid residues 61-106 of SEQ ID NO: 1", as recited in claim 18.

Furthermore, because recitation "substitutions, additions or deletions thereof" allows to completely replace the structure of "a peptide of from about 8 to about 25 amino acids", the instant invention encompasses a method of predicting efficacy of treatment of MS by administration of any peptide in existence. The instant specification fails to provide an adequate enabling disclosure for practicing such method of treatment and, consequently, one skilled in the art would not know how to practice a method of predicting efficacy of undisclosed method of treatment of MS.

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentec, Inc, v. Novo Nordisk*, 42 USPQ 2d 100,(CAFC 1997), the court held that:

"[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure". The court further stated that "when there is no disclosure of any specific starting material or of any of the conditions under which a

process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement".

The instant specification is not enabling because one cannot follow the guidance presented therein and practice the claimed method without first making a substantial inventive contribution.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 18-20 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 18-20 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in Paper No. 5 filed October 15, 2001. In that paper, applicant has stated that SEQ ID NO: 1is an amino acid sequence, which is 46 amino acids long, and this statement indicates that the invention is different from what is defined in the claim(s) because claim 18 encompasses a method of using a peptide having a sequence contained within amino acid residues 61-106 of SEQ ID NO: 1. Claims 19 and 20 depend from claim 18.

10. Claims 18-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. Claim 18 is vague and indefinite for recitation "from about 8 to about 25 amino acids". Even though the term "about" in a claim is inherently vague and indefinite, its use is appropriate when employed to limit a value, which is composed of indefinitely divisible units such as inches, meters, grams and pints where it is impractical to produce an item which has exactly the dimension recited. Even if one could practically produce an item, which is exactly 1 inch in length, the length of that item is conditional upon the temperature at which it is measured. However, when defining an invention in terms of indivisible numerical units such as the number of nucleotides in a nucleic acid, the number of amino acids in a polypeptide or the number of legs on a chair or table, the term "about" is unacceptably vague and indefinite since it is practical to employ a term, which possesses the required precision. If, for example, it is Applicant's intension that the claims should encompass a polypeptide of more than a certain amount of amino acids in length then this is exactly what the claim should recite. Whereas one would reasonably interpret the term "about one inch" as encompassing any value from 0.90 inches to 1.10 inches one would not know if the term "from about 8 to about 25 amino acids" would exclude 7 or 9 to 24 or 26 amino acids.

12. Claim 18 is further vague and indefinite for recitation "HLA-DR2 haplotype". It is suggested that the full name of the recitation is presented at first appearance of the acronym.

13. Claim 19 is vague and indefinite for recitation "DRB1*1501 or DRB1*15021". It is suggested that the full name of the recitation is presented in the claim.

14. Claim 20 is indefinite because it recites MS without providing a full name of the acronym. It is suggested that the instant abbreviation is included after the first recitation "a multiple sclerosis" in claim 18 to obviate this ground of rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.\

15. Claims 18-20 are directed to a method of predicting therapeutic efficacy of treatment of multiple sclerosis with a peptide of 8 to 25 amino acids from a fragment 61-106 of SEQ ID NO: 1, including substitutions, additions or deletions thereof, provided that the peptide is capable of neutralizing or modulating the production of anti-myelin basic protein, by screening a MS patient for the presence of an HLA-DR2 haplotype. If to assume that a peptide of 8 to 25 amino acids is a fragment of SEQ ID NO: 1, then the rejection under 35 U.S.C. 102 is as follows.

Claims 18-20 are rejected under 35 U.S.C. 102(e) as being anticipated by Guar et al. (US Patent 6,379,670, April 2002, filed on 08/19/1999). Gaur et al. disclose treatment of MS with peptide analogs of human myelin basic protein (column 13, lines 24-29). Such analogs include peptides "comprising at least 7 amino acids selected residues 83-99 of human myelin basic protein" (column 8. lines 51-52). Thus, the analog peptide of Guar et al. is the same peptide as the peptide disclosed on page 12, line 14 of the instant specification. Further, document of Guar et al. describes a method of identification of candidate patients for the disclosed method of treatment of MS (see column 14, lines 30-41), which encompasses identification of patients with

HLA-type DR2a and DR2b haplotypes, which have genetic predisposition to MS, and, therefore, would be candidates for the treatment. HLA-DR2 haplotype patients identified by disclosure of Guar et al. as suitable for the treatment would include patients carrying subtypes DRB1*1501 and DRB1*15021 because the disclosure of Guar et al. identified all HLA-DR2 haplotypes patients as responsive to treatment without exclusion of any specific subtype. Finally, because multiple sclerosis is generally defined as "a chronic, inflammatory disease" (column 1, lines 20-22), MS patients described by Guar et al. include patients with "chronic progressive MS". Thus, publication of Guar et al. meets the limitation of claims 18-20.

Conclusion

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Olga N. Chernyshev whose telephone number is (703) 305-1003. The examiner can normally be reached on Monday to Friday 9 AM to 5 PM ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on (703) 308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 782-9306 for regular communications and (703) 782-9307 for After Final communications.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices

published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)0. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556 or (703) 308-4242. If either of these numbers is out of service, please call the Group receptionist for an alternative number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Olga N. Chernyshev, Ph.D.
May 29, 2003